

## **Strain stimulus acting among migrating ameloblasts accounts for morphological features in human enamel**

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A theory is formulated to describe strain stimulus effects on the trajectories of migrating ameloblasts during the formation of dental enamel. Computer simulations reveal how the spatial patterns formed by the trajectories depend on the curvature of the surface (the dentin-enamel junction or DEJ) from which they begin to migrate and the parameters of the strain stimulus function that describes their response to variations in their separations during the migration. 1) The simulations account for the wave-like character of the trajectories of ameloblasts, which is linked to the lateral propagation of strain information across the growth front of the migration. 2) A transition is predicted from ordered to disordered behavior in regions where the DEJ is highly curved, in correspondence with the tortuous characteristics of gnarled enamel found under cusps. 3) Ameloblasts are inferred to have evolved strain response characteristics that place them on the verge of disordered behavior, which makes the enamel structure they create more responsive to changes in conditions and therefore more able to evolve for survival. 4) Since enamel morphology is the outcome of the collective behavior of ameloblasts, a small piece of enamel could only be correctly generated if ameloblasts are present in a volume much larger than that piece and in a geometrical context that is representative of nature. 5) Waviness and other morphological characteristics do not have any obvious explanation in chemical signaling alone. For generating enamel morphology, strain stimulus is the primitive signal; chemical signaling follows. 6) The simulations predict the onset of widespread compressive strain late in the migration, which is a possible signal for the cell die-off that terminates amelogenesis.